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Topological proteomics, toponomics, MELK-technology.

Schubert W.

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MELK is an ultrasensitive topological proteomics technology analysing proteins on the single cell level (Multi-Epitope-Ligand-'Kartographie'). It can trace out large scale protein patterns with subcellular resolution, mapping the topological position of many proteins simultaneously in a cell. Thereby, it addresses higher level order in a proteome, referred to as the toponome, coding cell functions by topologically and timely determined webs of interacting proteins. The resulting cellular protein maps provide new structures in the proteome: single combinatorial protein patterns (s-CPP), and combinatorial protein pattern motifs (CPP-motifs), bound to superior units. They are images of functional protein networks, which are specific signatures of tissues, cell types, cell states and diseases. The technology unravels hierarchies of proteins related to particular cell functions or dysfunctions, thus identifying and prioritising key proteins within cell and tissue protein networks. Interlocking MELK with the drug screening machinery provides new clues related to the selection of target proteins, and functionally relevant hits and drug leads. The present chapter summarizes the steps that have contributed to the establishment of the technology.

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1: Biochim Biophys Acta. 1997 Apr 11;1319(2-3):199-213.

The structural organization of the PsaC protein in Photosystem I from single crystal EPR and X-ray crystallographic studies.

Kamlowski A, van der Est A, Fromme P, Krauss N, Schubert WD, Klukas O, Stehlik D.

Institut fur Experimentalphysik, Freie Universitat Berlin, Germany.

In Photosystem I (PS I) the terminal electron acceptors, FA and FB, are iron-sulfur (4Fe-4S) centers, which are bound to the stromal subunit PsaC. The orientation of PsaC is determined relative to the whole PS I complex (see Schubert, W.-D. et al. (1995) in From Light to Biosphere (Mathis, P. ed.), Vol. II, pp. 3-10, Kluwer) from which a molecular model for the structure of PsaC within PS I is derived. Two strategies are followed: (i) PS I single crystal EPR data on the orientation of the g tensors of both FA- and FB- relative to each other and relative to the crystal axes (see preceding paper) are used in conjunction with the central structural part of the bacterial 2 [Fe4S4] ferredoxins, the cysteine binding motifs of which are known to be homologous to those of PsaC; (ii) the same core structure is fitted into the intermediate resolution electron density map of PS I. The PsaC orientation obtained both ways agree well. The local twofold symmetry axis inherent to the ferredoxin model leaves a twofold ambiguity in the structural conclusion. Deviations from this C2-symmetry in the amino acid sequence of PsaC are analyzed with respect to observable properties which would resolve the remaining structural ambiguity. Arguments both for and against FA being the distal iron-sulfur center (to FX) are discussed.

PMID: 9131044 [PubMed - indexed for MEDLINE]

1: Exp Mol Med. 2001 Apr 21;33(1 Suppl):5-18. Related Articles, Links

[Identification of proteome molecules by proteomics using two-dimensional gel electrophoresis and MALDI-TOF MS]

[Article in Korean]

Song EJ, Lee KJ.

College of Pharmacy and Divison of Molecular Life Sciences Ewha Womans University, Seoul, Korea.

Genomic technologies have enabled rapid accumulation of information from complex biological systems over the last two decades. The complete DNA sequence is now known for many organisms and the informational database obtained from genome sequencing projects has provided the base for the specification of proteome - the protein complement of genome. Genomic functions can be inferred from the analysis of gene structure and gene expression profiles because proteins are the functional molecules of an organism. Integrated technologies including protein separation, identification, characterization and information manage system are essential to analyze the proteins in complex cellular matrix. This study is focusing on the strategies of proteome analysis using sample preparation, 2-dimensional gel electrophoresis, processing of protein spots and identification of proteins, protein-protein interaction and posttranslational modification using MALDI-TOF-MS. 2-D gel electrophoresis is currently the most powerful protein separation technique and MALDI-TOF MS is powerful identification technique for protein and peptides as a sensitive, rapid, and high resolution analytical method. The developed integrated proteome technologies are very useful to understand the biological phenomena at molecular level by identifying the new molecules and their modifications in various cellular processes, and can be applied for biotechnology including medical science.

PMID: 11708325 [PubMed - indexed for MEDLINE]

nature

nature 26 April 1990

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Nature **344**, 868 - 870 (1990); doi:10.1038/344868a0

Activin is a nerve cell survival molecule

D. Schubert, H. Kimura, M. LaCorbiere, J. Vaughan, D. Karr & W. H. Fischer

THE structures of five neurotrophic molecules have so far been published. Nerve growth factor[1], fibroblast growth factor[2, 3] and purpurin[4], have been identified as nerve-cell survival molecules. More recently, brain-derived neurotrophic factor (BDNF) and ciliary neurotrophic factor have been cloned and sequenced[5, 6]. As all these proteins stimulate the survival of ciliary or sensory neurons, a new cell survival assay is required if novel neurotrophic molecules are to be discovered. P19 teratoma cells differentiate to nerve-like cells in the presence of 5×10^{7} M retinoic acid (RA)[7, 8]. But when P19 cells are plated in N^2 synthetic medium[9] without being exposed to RA, they die within 48 h. In an attempt to identify a molecule(s) that can substitute for RA in promoting P19 survival, we assayed serum-free growth-conditioned media for their ability to promote P19 survival. One cell line from the rat eye secreted a molecule that promoted the survival of P19 cells and some types of nerve cell. We identified this molecule as activin, better known for its role in hormone secretion.

Schubert et al.
Nature 344: 868 1990